REMARKS

Status of the claims

Claims 6, 7, 9, 49, and 50 are under consideration in this application, claims 1-5, 8, and 10-48 having been withdrawn from consideration for allegedly being drawn to separate inventions and claims 49 and 50 having been added herein. Claims 49 and 50 are supported by the specification, e.g., at page 8, lines 13-14, Fig. 2B, page 3, lines 11-13, and Examples 3-5. Neither the amendments to the claims already under consideration (see below) nor the new claims add new matter.

35 U.S.C. §112, first paragraph, rejections

Claims 6, 7, and 9 stand rejected: (a) on the grounds that the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims; and (b) as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the application was filed, had possession of the claimed invention.

While disagreeing with the Examiners position that the specification neither enables nor provides adequate written description of the claimed polypeptides, in order to expedite prosecution of the instant application, Applicant has amended the claims and added additional claims so as to further limit the overall range of polypeptides encompassed by the claims and hence also the experimentation one of skill in the art would need to perform in order to make the polypeptides. The amendments to claims 6, 7 and 19 are supported throughout the specification, e.g., at 16, lines 6-8, and page 18, lines 10-12.

With respect to the comments on page 4, lines 11-29, of the Office Action, claim 6 has been amended to specify particular hybridization conditions that, as indicated by the specification (e.g., at page 16, lines 6-8), are "highly stringent" conditions. As acknowledged by the Examiner, the stringency conditions significantly limit the "variation between two hybridizing sequences" (Office Action, page 4, lines 17-18).

With regard to the comment on page 4, line 20, of the Office Action, the claims do contain a functional limitation ("the ability to costimulate a T cell") that, as argued below, is both well-defined and readily testable. Moreover, contrary to the Examiner's assertion on page 5, lines 23-25, of the Office Action, the term "ability to costimulate a T cell") does not, also as pointed out below, encompass "numerous and mutually exclusive functions."

In regard to the comments on page 4, lines 30-35, of the Office Action, Applicants have limited the number of conservative substitutions within any given polypeptide to between 1 and 10. This amendment, which is supported by the specification (e.g., at page 18, lines 10-12), even further restricts the range of polypeptides encompassed by the claims. Experimentation necessary to determine whether a polypeptide with a given conservative substitution, or set of conservative substitutions, has the requisite costimulatory activity would, given the teaching of the instant specification (e.g., Examples 1, 3-5, 8, 9, and 10-12) and the knowledge of one skilled in the art, be entirely routine for such an artisan. The Examiner is reminded that:

> a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable guidance with respect to the direction in which experimentation should proceed. *In re Wands*, 858 F.2d 731, 736-7 (Fed. Cir. 1988).

With respect to the comments on page 4, lines 36-46, of the Office Action, Applicant has changed references to SEQ ID NOs from the term "an amino acid sequence of..." to "the amino acid sequence set forth in..." Nevertheless, claims 6, 7, 49, and 50 cover fragments that are supported in terms of both enablement and written description by the specification (see above). Moreover, by inspection of the diagrammatic representations of the B7-H1 molecule in Figures 2A and 2B, and the text on, for example, page 3, lines 11-13, of the specification, one skilled in the art would be appraised of multiple polypeptide fragments (in addition to those specifically claimed) that would fall within the functional and structural embodiments of the claims.

In light of the above considerations, Applicant respectfully submits that the specification provides: (1) teaching sufficient to allow one of skill in the art to practice the invention without undue experimentation; and (2) sufficient specific examples of polypeptides encompassed by

both the generic and species claims. Thus, Applicant respectfully requests withdrawal of the rejections under 35 U.S.C. §112, first paragraph.

35 U.S.C. §112, second paragraph, rejection

Claims 6, 7, and 9 stand rejected as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

By amending claim 6 to be in independent form, rejection (A) is rendered moot.

With respect to rejection (B), Applicant has amended the claims to employ the term "a polypeptide with the amino acid sequence set forth in..." suggested by the Examiner and thus the rejection is moot.

With respect to rejection (C), Applicant has amended claim 6 to include one of the hybridization parameters disclosed on page 16 of the specification and to which the Examiner referred in the rejection. Thus, the rejection is moot.

With respect to rejection (D), Applicant respectfully submits that the term "ability to costimulate a T cell" is not indefinite for referring to mutually exclusive functions. As indicated by the definition on page 6, lines 21-29, of the specification, the term "costimulate" always refers to the enhancement of a T cell response. If, for example, the T cell in question is a helper T cell, then helper activity of the T cell developed in its response is enhanced by costimulation. On the other hand, if the T cell is a suppressor T cell, then suppressive activity of the T cell developed in its response is enhanced by the costimulation. Assays for these activities of T cells, and for enhancement of responses resulting these activities, are known in the art. Applicant also draws the Examiner's attention to the fact that term "ability to costimulate a T cell" is a functional limitation in the claims of issued U.S. Patent No. 5,858,776 cited by the Examiner.

In light of the above considerations, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

35 U.S.C. §102(e) rejection

Claim 6 stands rejected as allegedly being anticipated by Ostrand-Rosenburg et al. (U.S. Patent No. 5,858,776; the "'776 patent"). Applicant respectfully traverses the rejection.

In regard to the comments on page 7, lines 23-32, of the Office Action, Applicant draws the Examiner's attention to the fact, while the extracellular domain of B7-H1 has about 20% amino acid identity to the polypeptide disclosed in the '776 patent (designated B7-1 in the instant application; see page 8, line 14, and Fig. 2B), the intracellular domain of B7-H1 is "highly divergent" from that of B7-1. Moreover, to observe even the relatively low 20% amino acid identity of the extracellular domains, both the B7-H1 and B7-1 amino acid sequences had to be "gapped" at multiple sites (see Fig. 2B of the instant application). In view of these factors, Applicant submits that, in that the '776 patent's nucleic acid sequence (SEQ ID NO:1) would be highly unlikely to hybridize under the highly stringent conditions specified by claim 6 to any of the nucleic acid sequences embodied by instant claim 6, the '776 patent's polypeptide (SEQ ID NO:2) encoded by the '776 patent's SEQ ID NO:1 does not anticipate the polypeptides specified by the instant claims. Applicant draws the Examiner's attention to the fact that the '776 patent does not disclose any specific fragments of its SEQ ID NO:1 or SEQ ID NO:2 molecules.

In light of the above considerations, Applicants request that rejection under 35 U.S.C. §102(e) be withdrawn.

Attached is a marked-up version of the changes being made by the current amendment.

CONCLUSIONS

Applicant submits that the pending claims patentably define the invention. Applicant requests that the Examiner reconsider the rejections set forth in the Office Action, and permit the pending claims to pass to allowance.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's undersigned representative can be reached at the telephone number listed below.

Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 10/15/02

Stuart Macphail, Ph.D.
Reg. No. 44,217

Fish & Richardson P.C.
45 Rockefeller Plaza, Suite 2800
New York, New York 10111
Telephone: (212) 765-5070
Facsimile: (212) 258-2291

Version with markings to show changes made

In the specification:

On page 1, line, delete the title ("B7-H1, A NOVEL IMMUNOREGULATORY MOLECULE") and replace it with --B7-H1, AN IMMUNOREGULATORY MOLECULE--

Amend the paragraph beginning on page 15, line 18, as follows:

The determination of percent identity between two sequences is accomplished using the mathematical algorithm of Karlin and Altschul, *Proc. Natl. Acad. Sci USA* 90, 5873-5877, 1993. Such an algorithm is incorporated into the BLASTN and BLASTP programs of Altschul et al. (1990) *J. Mol. Biol.* 215, 403-410. BLAST nucleotide searches are performed with the BLASTN program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to B7-H-1-encoding nucleic acids. BLAST protein searches are performed with the BLASTP program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to B7-H1. To obtain gapped alignments for comparative purposes, Gapped BLAST is utilized as described in Altschul et al. (1997) *Nucleic Acids Res.* 25, 3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) are used [(*See* http://www.ncbi.nlm.nih.gov)].

In the claims:

Claims 6, 7 and 9 have been amended as follows:

6. (Amended) An isolated polypeptide encoded by [the] a DNA [of claim 1] comprising a nucleic acid sequence that encodes a polypeptide with the ability to co-stimulate a T cell, wherein the nucleic acid sequence hybridizes, after a wash at 65°C in a buffer containing 0.2 x SSC and 0.1% SDS, to the complement of a sequence that encodes a polypeptide with the amino acid sequence set forth in SEQ ID NO:1.

7. (Amended) The isolated polypeptide of claim 6, wherein the polypeptide comprises [an amino acid sequence of] amino acid residue 23 to amino acid residue 290 of the amino acid sequence set forth in SEQ ID NO:1, or [said amino acid sequence] amino acid residue 30 to amino acid residue 290 of the amino acid sequence set forth in SEQ ID NO:1 but differing solely by 1-10 conservative substitutions.

9. (Amended) The isolated polypeptide of claim 6, wherein the polypeptide comprises [an] the amino acid sequence set forth in SEQ ID NO:1, or [said amino acid sequence] the amino acid sequence set forth in SEQ ID NO:1 but differing solely by 1-10 conservative substitutions.

Claims 49 and 50 are added.

--49. The isolated polypeptide of claim 6, wherein the polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 10, or the amino acid sequence set forth in SEQ ID NO:10 but differing solely by 1-10 conservative substitutions.

50. The isolated polypeptide of claim 49, wherein the polypeptide comprises amino acid residue 23 to amino acid residue 290 of the amino acid sequence set forth in SEQ ID NO:1, or amino acid residue 23 to amino acid residue 290 of the amino acid sequence set forth in SEQ ID NO:1 but differing solely by 1-10 conservative substitutions.--

In the abstract:

Amend the abstract as follows.

The invention provides [novel] polypeptides useful for co-stimulating T cells, isolated nucleic acid molecules encoding them, vectors containing the nucleic acid molecules, and cells containing the vectors. Also included are methods of making and using these co-stimulatory polypeptides.